

WHAT IS CLAIMED IS:

1. A method of specifically inhibiting growth of tumor cells that overexpress an RRP protein comprising contacting said tumor cells with an amount of an exogenous RRP binding agent that results in inhibition in growth of tumor cells.
2. The method of claim 1 wherein said tumor cells are from a tissue selected from the group consisting of breast, ovary, lung, kidney, and colon.
3. The method of claim 1 wherein said RRP binding agent is an antibody or a fragment of said antibody.
4. The method according to claim 3 wherein said antibody is humanized.
5. The method according to claim 3 wherein said antibody comprises human constant region residues and rhomboid-specific mouse variable region residues.
6. The method according to claim 3 wherein said antibody is bound to a detectable label.
7. The method according to claim 3 wherein said antibody is bound to a cytotoxic label.
8. A method of screening for agents that modulate the interaction of an RRP polypeptide with an RRP binding target, comprising:
  - a) expressing a recombinant RRP polypeptide,
  - b) incubating the recombinant RRP polypeptide with an RRP binding target and a candidate RRP modulating agent and
  - c) determining whether said candidate RRP modulating agent modulates the binding of the RRP polypeptide with the RRP binding target.
9. The method according to claim 8 wherein said binding target is selected from the group consisting of TGF $\alpha$ , EGF, and amphiregulin.
10. The method according to claim 8 wherein said binding target is TGF $\alpha$ .

11. The method according to claim 8 wherein said candidate RRP modulating agent is an antibody.
12. The method according to claim 8 wherein said candidate RRP modulating agent is a small organic molecule.
13. A method of diagnosing a tumor cell as having abnormal p53 or p21 pathway signaling, comprising measuring RRP expression levels in said tumor cell, wherein increased RRP expression levels in the tumor cell compared to a non-tumor cell of the same tissue or organ as the tumor cell, indicates defective p53 or p21 pathway signaling in the tumor cell.
14. A method of identifying a candidate p53 or p21 pathway modulating agent, said method comprising the steps of:
  - a) providing an assay system comprising a purified RRP polypeptide or nucleic acid or a functionally active fragment or derivative thereof;
  - b) contacting the assay system with a test agent under conditions whereby, but for the presence of the test agent, the system provides a reference activity; and
  - c) detecting a test agent-biased activity of the assay system, wherein a difference between the test agent-biased activity and the reference activity identifies the test agent as a candidate p53 or p21 pathway modulating agent.
15. The method of Claim 14 wherein the assay system comprises cultured cells that express the RRP polypeptide.
16. The method of Claim 15 wherein the cultured cells additionally have defective p53 or p21 function.
17. The method of Claim 14 wherein the assay system includes a screening assay comprising a RRP polypeptide, and the candidate test agent is a small molecule modulator.
18. The method of Claim 17 wherein the assay is a protease assay.

19. The method of Claim 14 wherein the assay system is selected from the group consisting of an apoptosis assay system, a cell proliferation assay system, an angiogenesis assay system, and a hypoxic induction assay system.
20. The method of Claim 14 wherein the assay system includes a binding assay comprising a RRP polypeptide and the candidate test agent is an antibody.
21. The method of Claim 14 wherein the assay system includes an expression assay comprising a RRP nucleic acid and the candidate test agent is a nucleic acid modulator.
22. The method of claim 21 wherein the nucleic acid modulator is an antisense oligomer.
23. The method of Claim 21 wherein the nucleic acid modulator is a PMO.
24. The method of Claim 14 additionally comprising:  
d) administering the candidate p53 or p21 pathway modulating agent identified in (c) to a model system comprising cells defective in p53 or p21 function and, detecting a phenotypic change in the model system that indicates that the p53 or p21 function is restored.
25. The method of Claim 24 wherein the model system is a mouse model with defective p53 or p21 function.
26. A method for modulating a p53 or p21 pathway of a cell comprising contacting a cell defective in p53 or p21 function with a candidate modulator that specifically binds to an RRP polypeptide comprising an amino acid sequence selected from group consisting of SEQ ID NOs:2, 4, 6, 8, 10, 12, 14, 16, and 46 whereby p53 or p21 function is restored.

27. The method of claim 26 wherein the candidate modulator is administered to a vertebrate animal predetermined to have a disease or disorder resulting from a defect in p53 or p21 function.
28. The method of Claim 26 wherein the candidate modulator is selected from the group consisting of an antibody and a small molecule.
29. The method of Claim 14, comprising the additional steps of:
- e) providing a secondary assay system comprising cultured cells or a non-human animal expressing RRP ,
  - f) contacting the secondary assay system with the test agent of (b) or an agent derived therefrom under conditions whereby, but for the presence of the test agent or agent derived therefrom, the system provides a reference activity; and
  - g) detecting an agent-biased activity of the second assay system,
  - h) wherein a difference between the agent-biased activity and the reference activity of the second assay system confirms the test agent or agent derived therefrom as a candidate p53 or p21 pathway modulating agent,
  - i) and wherein the second assay detects an agent-biased change in the p53 or p21 pathway.
30. The method of Claim 29 wherein the secondary assay system comprises cultured cells.
31. The method of Claim 29 wherein the secondary assay system comprises a non-human animal.
32. The method of Claim 31 wherein the non-human animal mis-expresses a p53 or p21 pathway gene.

33. A method of modulating p53 or p21 pathway in a mammalian cell comprising contacting the cell with an agent that specifically binds a RRP polypeptide or nucleic acid.
34. The method of Claim 33 wherein the agent is administered to a mammalian animal predetermined to have a pathology associated with the p53 or p21 pathway.
35. The method of Claim 33 wherein the agent is a small molecule modulator, a nucleic acid modulator, or an antibody.
36. A method for diagnosing a disease in a patient comprising:
- a) obtaining a biological sample from the patient;
  - b) contacting the sample with a probe for RRP expression;
  - c) comparing results from step (b) with a control;
  - d) determining whether step (c) indicates a likelihood of disease.
37. The method of claim 36 wherein said disease is cancer.
38. The method of claim 37, wherein said cancer is a cancer as shown in Table 1 as having >25% expression level.
39. A purified nucleic acid molecule that encodes a polypeptide comprising an amino acid sequence as set forth in SEQ ID NO:46, or reverse complement thereof.
40. The nucleic acid molecule of Claim 39 which is capable of hybridizing to a nucleic acid sequence of SEQ ID NO:45 using high stringency hybridization conditions.
41. A recombinant expression system comprising a DNA or RNA molecule, wherein said expression system is capable of producing an mRRP1 polypeptide comprising the amino acid sequence of SEQ ID NO:46 when said expression system is present in a compatible host cell.
42. A host cell comprising the expression system of claim 41.

43. A process for producing an mRRP1 protein comprising culturing the host cell of Claim 42 under conditions suitable for expression of said mRRP1 protein and recovering said protein.
44. A process for producing a cell which produces an mRRP1 protein comprising the transformation or transfection of a host cell with the expression system of claim 41 such that the host cell, under appropriate culture conditions, produces an mRRP1 protein.
45. A recombinant host cell expressing the protein produced by the method of claim .
46. A transgenic mouse whose genome comprises a disruption in an endogenous RRP gene wherein said disruption results in decreased expression or a lack of expression of said endogenous RRP gene.
47. The mouse of claim 46, wherein said mouse is homozygous for the disrupted RRP gene.
48. A cell isolated from the transgenic mouse of claim 46.
49. A mouse cell whose genome comprises a disruption in an endogenous RRP gene wherein said disruption results in decreased expression or a lack of expression of said endogenous RRP gene.
50. A method of selecting an agent that modulates cell proliferation comprising:
- a) providing a first and a second isolated mouse cell wherein the genome of both the first and second isolated mouse cell has been manipulated to comprise a disruption in an endogenous RRP gene wherein said disruption results in decreased expression or a lack of expression of said endogenous RRP gene;
  - b) administering an agent to said first isolated mouse cell ; and

- c) determining the amount of proliferation of the first and second cell, wherein a difference in the amount of proliferation of the first cell as compared to the second cell indicates that the agent modulates cell proliferation.

51. A method of making an antibody against a human RRP comprising:

- a) injecting RRP or an antigenic fragment thereof to mouse of claim 46; and
- b) recovering said antibody.